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Influence of tramadol on anesthesia times, analgesia and electrocardiogram associated with injection anesthesia in common buzzards (*Buteo buteo*)

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Abstract

A balanced anesthesia protocol is called perfect when it has fast induction, excellent recovery, the least effect on the cardiopulmonary system and sufficient analgesia. Many of anesthetic combinations have an analgesic effect without opioids. However, at the end of anesthesia, analgesia decreases or is incomplete**.** The purpose of this study was to evaluate anesthesia times, electrocardiogram (ECG) and analgesic effect of tramadol when administrated with ketamine, ketamine-diazepam, ketamine-midazolam, and ketamine-xylazine and selected a balanced anesthesia protocol in buzzards. Ten adult common buzzards (*Buteo buteo*) received seven different anesthetic protocols (with or without tramadol). In each protocol, anesthesia times, electrocardiograph parameters and analgesic effect were recorded. Excluding ketamine-tramadol, all protocols produced deep anesthesia in all buzzards. Among of all protocols, no significant differences regarding the amplitude and duration of waves (P, QRS and T) was found. By adding tramadol to anesthetic protocols, response duration to thermal sense increased up 3 hr after recovery. Tramadol did not make considerable effects on anesthesia times and ECG and made analgesic effect up to 3 hr when used with ketamine-benzodiazpins or ketamine-xylazine. Therefore, tramadol can be used with injectable anesthetics to make suitably balanced anesthesia in buzzards.

اثر ترامادول بر روی زمان‌های بیهوشی، بی دردی و الکتروکاردیوگرام همراه با بیهوشی تزریقی در سارگپه معمولی (*Buteo buteo*)

چکیده

یک روند بیهوشی متعادل، زمانی کامل است که دارای القا سریع، برگشت از بیهوشی عالی، کمترین اثر بر دستگاه قلبی ریوی و بی دردی کافی باشد. ترکیبات بیهوشی متعددی بدون داروهای ضد درد مخدر، بی دردی ایجاد می کنند. اگرچه، بی دردی در انتهای بیهوشی کاهش می یابد یا ناقص است. هدف این مطالعه، ارزیابی زمانهای بیهوشی، الکتروکاردیوگرام و اثر بی دردی ترامادول هنگامی که همراه با کتامین، کتامین – دیازپام، کتامین– میدازولام و کتامین– زایلازین تزریق شود و انتخاب یک روند بیهوشی متعادل در سارگپه ها بود. تعداد ۱۰ بهله سارگپه معمولی بالغ، ۷ تیمار از روندهای بیهوشی را دریافت کردند (همراه با ترامادل یا بدون آن). برای هر روند بیهوشی، زمان‌های بیهوشی، فراسنجه های الکتروکاردیوگراف و اثر بی دردی ثبت گردید. به جز ترکیب کتامین– ترامادول، همه روندهای بیهوشی در تمام سارگپه ها، بیهوشی عمیقی ایجاد کردند. تفاوت معناداری در ارتفاع و طول موجهای P، QRS و T در بین روندهای بیهوشی وجود نداشت. با اضافه کردن ترامادول به روندهای بیهوشی، طول پاسخ به حس گرما تا سه ساعت بعد از برگشت از بیهوشی افزایش یافت. ترامادول وقتی همراه با کتامین–بنزودیازپین ها یا کتامین – زایلازین در سارگپه استفاده شد، آثار قابل توجه ای بر زمان‌های بیهوشی و الکتروکاردیوگرام نداشت و اثر بی دردی بیش از ۳ ساعت ایجاد کرد. بنابراین، ترامادل می تواند همراه با داروهای بیهوشی تزریقی برای ایجاد یک بیهوشی متعادل در سارگپه مورد استفاده قرار گیرد.

واژه های کلیدی: بیهوشی متعادل، ترامادل، داروهای بیهوشی تزریقی، سارگپه

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Introduction

A balanced anesthesia protocol must have high-quality characters including fast induction, excellent recovery, sufficient analgesia and minimum effects on the cardiopulmonary system.[1] Inhalation anesthesia has these characters in birds and other animals, however, it has several limitations therefore injectable anesthesia is applied for chemical immobilization as an alternative.[2] Sedation, anesthesia and analgesia in birds are performed by drugs such as isoflurane, ketamine, benzodiazepines, α_2 agonists and opioids.[3-7] In some procedures in birds (diagnostic imaging) that are not usually associated with pain, analgesia is not essential and muscle relaxation or sedation can be enough.[8] While, in painful or invasive procedures, balanced anesthesia should be performed to induce analgesia.[9,10] When ketamine is combined with benzodiazepines or xylazine, analgesic effect is sufficient during the anesthesia,[9,11] but, for stabling the surgical patient status and decreasing pain, an analgesic drug can be useful. Tramadol has been used in bald eagles, red-tailed hawks, kestrels, Hispaniola Amazon parrots and chickens in a single dose or with ketamine.[12-19] In many of these studies, tramadol has been administrated orally and the birds have been restrained manually and this restraint was unsafe for them.[20] For postoperative management of the pain in avian patients, analgesic drugs can be used with the following properties: combination with anesthetic drugs and long analgesic effects without any side effects on the cardiopulmonary system.

The purpose of the present study was to evaluate anesthetic times, electrocardiogram (ECG) changes and analgesic effect of tramadol when administrated with ketamine, ketamine-benzodiazepines, and ketamine-xylazine and choose a balanced anesthesia protocol in common buzzards (*Buteo buteo*).

Materials and Methods

Ten adult common buzzards of unknown sexes with 1500.60 ± 240.40 g body weight obtained from Lorestan Environmental Protection Office in Khorramabad, Lorestan, Iran were used in this study. All buzzards were captive bred and determined to be healthy on the basis of physical examinations performed before and during the study. The buzzards were housed in individual cages (100 × 100 × 100 cm) in a quiet room in the hospital to avoid possible stress-inducing factors during the study and fed a meat-based diet in accordance with the previous feeding regimen. The buzzards had free access to water and food except for 3 hr prior to the experiment. The study protocol was approved by the Institutional Animal Care and Use Committee of the Lorestan University, Khorramabad, Iran (ethical code: LU.ECRA.2016.1).

Anesthesia. A within-subject, complete cross-over experimental design was used for this study. Each of the 10 buzzards received treatments with a washout period of two weeks. Treatments were intra-muscular administration of ketamine 10.00% (30 mg kg^{-1}; Alfasan, Woerden, Netherlands)-tramadol (4 mg kg^{-1}; Chemidarou, Tehran, Iran), [KT], ketamine (30 mg kg^{-1})-xylazine (1 mg kg^{-1}; Alfasan), [KX], ketamine (30 mg kg^{-1})-diazepam (0.20 mg kg^{-1}; Daroupakhsh), [KD], ketamine (30 mg kg^{-1})-midazolam (0.20 mg kg^{-1}; Daroupakhsh, Tehran, Iran), [KM], ketamine-diazepam-tramadol (4 mg kg^{-1}), [KDT], ketamine-midazolam-tramadol (4 mg kg^{-1}), [KMT] and ketamine-xylazine-tramadol (4 mg kg^{-1}), [KXT] which were based on previous studies in raptor birds.[5,12] Birds were given tramadol immediately after administration of ketamine, ketamine-benzodiazepines or ketamine-xylazine combination. Drugs were administered intra-muscularly at the deep pectoral muscle using insulin injector.

The onset time, anesthesia time and complete recovery time were subjectively evaluated based on standard tests.[4,21-23] The onset time was defined as the time between drug administration and early signs of the bird's reaction to sedation including the closure of the eyelids and falling of wings and tail. The anesthesia time was defined as the duration of loss of righting reflexes such as lack of voluntary movement and no response to postural changes. Complete recovery time was defined as the time from returning of the righting reflex to complete standing of birds. The quality of recovery was divided into excellent, good and poor indices based on a previous study.[24] Excellent recovery was defined as a status in which the bird showed early sternal position with little or no struggle, walking without assistance or struggle, not falling to sternal recumbency once standing and minimal ataxia during walking. Good recovery was defined as a status in which the birds showed sternal position with little or no struggle, premature standing without weakness in hind limbs, not to fall to sternal recumbency unlikely once standing and slight ataxia. Poor recovery was defined as a status in which the birds showed some struggling, repeated attempts to move from lateral to sternal recumbency, premature standing with splayed and weak hind limbs, repeatedly falls to sternal recumbency once standing, manual restraint required to avoid injury.

ECG recording. The ECG recording was taken in three anesthetic planes under light anesthesia.[22] Alligator clip electrodes were attached to the wing web at the base of the right and left wings and at the right and left thighs near the proximal attachment of the gastrocnemius muscle. Electrode gel was used for an adequate contact establishment. The ECGs were recorded by a digital electrocardiograph (Kenz 110; Suzuken, Nagoya Japan) and all recordings were calibrated to 1 mV/10 mm, with a paper speed of 50 mm sec^{-1}. We recorded standard bipolar (I, II, and III) and augmented unipolar (aVR, aVL, and aVF) leads. The duration

and amplitude of waves on the trace were measured in the lead II and mean electrical axis of ventricular depolarization in the frontal plane was calculated using the leads II and III. Measurement of the heart rate was also carried out in the lead II[25]. Arrhythmias in the electrocardiographs were blindly evaluated by a cardiologist.

Thermal nociceptive testing procedure. Measurements of head and foot reaction to heat were performed for all buzzards based on Hothersall *et al*. method with some modifications.[26] Briefly, a test box equipped with a thermal probe attached to digital hot plate was used. The probe contained a heater element connected by a ribbon cable to the digital hot plate. The probe was attached to the skin of the left leg in each bird. We evaluated different temperatures (30, 35, 40, 45 and 50 ˚C) in all conscious buzzards in a pilot study. The response time of each buzzard to heat of probe after reaching of the probe and a hot plate to the determined standard temperature was recorded. For the main study, a temperature was chosen in which response of all buzzards to heat was shorter than 5 sec and there were no signs of inflammation or tissue damage on buzzard skin. The standard temperature used for the study was 45 ˚C. Thermal testing was performed in five different times for each anesthetic protocol. These times were evaluated 1 hr before anesthesia, during anesthesia and 30, 90 and 180 min after recovery.

A pilot study showed that buzzards, like other birds, could lift their foot and head via withdrawal where the heat was felt. We recorded time of lifting of leg or withdrawing of the head after the temperature of the probe got to 45 ˚C. We graded quality of analgesia to excellent (reaction after 10 sec), good (reaction between 5 to 10 sec) and poor (reaction shorter than five sec).

Statistical analysis. All results were analyzed using the SPSS (version 19.0; SPSS Inc., Chicago, USA). Data were collected regarding the onset and duration of sedation and duration of dorsal recumbency and ECG data were analyzed using a one-way ANOVA followed by a Duncan test, when appropriate. All the measurements were expressed as mean ± SEM and differences were considered significant at a value of $p < 0.05$.

Results

Anesthesia was produced in all birds following intramuscular administration of the anesthetic agents. The onset, duration and complete recovery of each treatment are shown in Figure 1. As can be seen, induction time was shorter in KD (2.10 ± 0.22 min), KT (2.30 ± 0.14 min), KX (2.70 ± 0.44 min) and KXT (2.90 ± 0.22 min) in comparison with other treatment protocols. However, a significant difference was only observed in the induction time of KD and KT treatment protocols compared to that of other treatment protocols ($p < 0.05$). The duration of anesthesia was long in the KXT (80.60 ± 3.97 min), KX (83.80 ± 3.96 min), and KD (84.20 ± 3.27 min) treatment protocols, whereas it was short in the KDT (48.00 ± 4.47 min), KM (48.20 ± 4.38 min), KMT (39.80 ± 6.06 min) and KT (15.80 ± 3.06 min) treatment protocols. However, the duration of anesthesia was not calculated in four buzzards in the KT treatment protocol because they did not remain in dorsal recumbency. Briefly, there were no significant differences in the duration of anesthesia between the KX, KXT and KD treatment protocols ($p > 0.05$). Also, the difference of anesthesia times between the KDT, KM and KMT treatment protocols was similar to those in the KX, KXT and KD treatment protocols ($p > 0.05$). However, a significant difference in anesthesia times was revealed between KT and other groups.

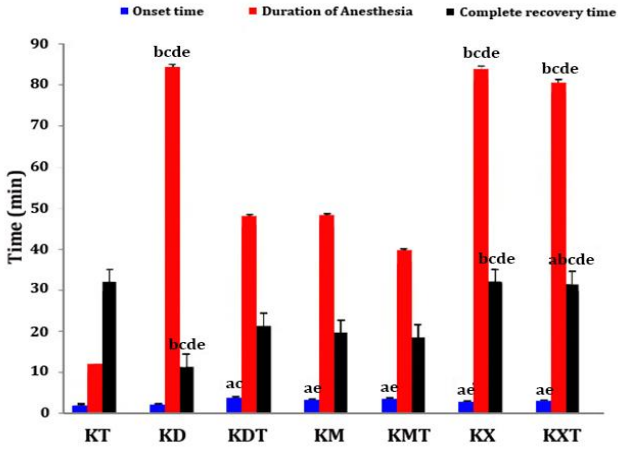

Fig. 1. Influence of tramadol on anesthesia times when administrated immediately after ketamine-benzodiazpins or xylazine : Ketamine (K), Xylazine (X), Diazepam (D), Midazolam (M), Tramadol (T) in common buzzards (*Buteo buteo*). [a] p <0.05 vs KD treatment protocol, [b] p <0.05 vs KDT treatment protocol, [c] p <0.05 vs KM treatment protocol, [d] p <0.05 vs KMT, [e] p <0.05 vs KT.

The shortest recovery time was obtained in the KD (11.20 ± 3.76 min) treatment protocol and the longest recovery time was observed in the KT (32.00 ± 5.80 min), KX (32.00 ± 3.80 min) and KXT (31.40 ± 2.70 min) treatment protocols. Data analyses showed significant differences in recovery times between the KT, KX and KXT treatment protocols and other experimental treatment protocols ($p < 0.001$). The quality of recovery is shown in Table 1.

Table 1. The evaluation of recovery quality in the experimental groups (number of buzzards).

Protocols	Excellent	Good	Poor
KX	0	5	5
KXT	2	5	3
KD	0	6	4
KDT	2	6	2
KM	1	6	3
KMT	2	6	2
KT	0	3	7

KT: Ketamin-Tramadol, KM: Ketamine-Midazolam, KD: Ketamine-Diazepam, KX: Ketamine-Xylazine, KMT: KM-Tramadol, KDT: KD-Tramadol, KXT: KX-Tramadol.

Briefly, the quality of recovery was good in KD, KM, KDT, KXT and KMT treatment protocols and it was poor in the KX and KT treatment protocols.

Arrhythmia was observed only in a single bird anesthetized with KX (Fig. 2). The ECG results for the experimental protocols are shown in Table 2. There was no significant difference regarding the amplitude and duration of waves (P, QRS and T) among the treatment protocols. However, results indicated significant differences in the heart rate between the KX and the other treatment protocols ($p < 0.05$) except for the KXT. Moreover, there was a significant difference in the heart rate between the KXT treatment protocol and the other treatment protocols ($p < 0.05$).

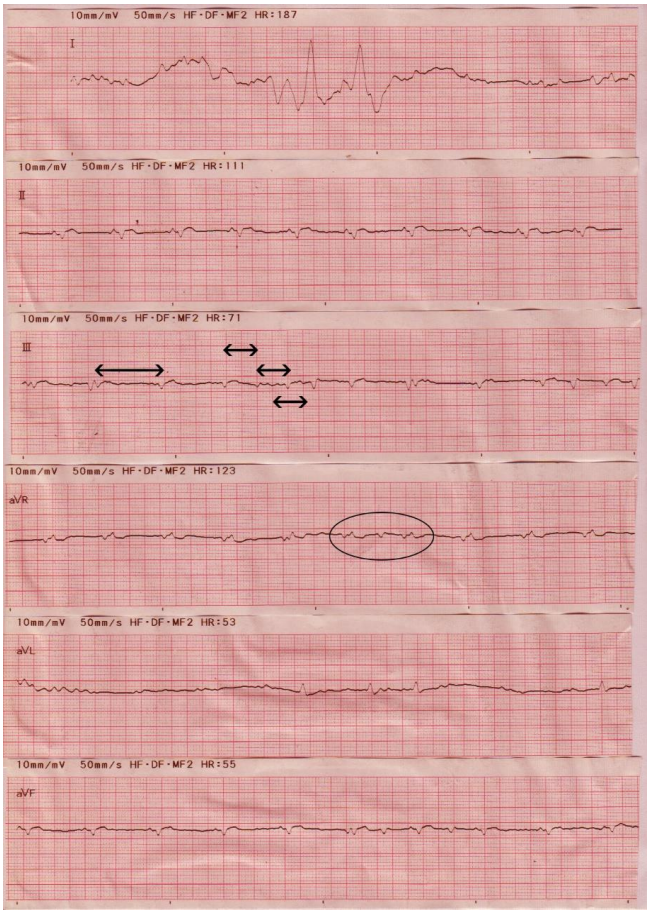

Fig. 2. Electrocardiograph of the buzzard after anesthesia with ketamine-xylazine in six leads. Standardization, 10 mm 51 mV; chart speed, 50 mm sec^{-1}. Cardiac arrhythmia in lead III and aVR has been shown.

The quality of analgesia at different times is shown in Table 3. By adding tramadol to anesthesia treatment protocols, response duration to thermal sense was increased up to 180 min after recovery. Briefly, during anesthesia, analgesia in KT, KX, KXT, KDT, and KMT was better than KD and KM groups. In 30, 90 and 180 min after recovery, analgesia in KX, KD, and KM groups decreased with higher speed compared to other groups. On the whole, the addition of tramadol to injection anesthesia increased the quality of analgesia during anesthesia and 30, 90 and 180 min after recovery from anesthesia.

Discussion

In this study, the experimental treatment protocols produced anesthesia and analgesia to some extent in the buzzards. But, ketamine-tramadol combination failed to make all anesthesia planes in all buzzards. There are many antinociception and pharmacokinetic studies on tramadol in birds.[12-18] Antinociception and pharmacokinetic studies on tramadol in birds have been based on a thermal design and serum levels concentrations of O-desmethyltramadol, respectively.[27] Analgesia effect of tramadol is different in various doses. For example, in kestrels, between the doses of 5.00, 15.00 and 30.00 mg kg^{-1} of tramadol given orally, only the dose of 5.00 mg kg^{-1} increased analgesia, but the dose of 30.00 mg kg^{-1} decreased it.[16] Conversely, in the Hispaniolan Amazon parrots, oral administration of 30.00 mg kg^{-1} of tramadol had an analgesic effect compared to its 10.00 and 20.00 mg kg^{-1}.[17] Also, there is a wide variability of pharmacokinetic information concerning tramadol and its primary metabolite in avian species. Based on these data, the authors suggested different doses and methods in the birds.[27] In this study, following intra-muscular administration of 4 mg kg^{-1} tramadol, the quality of analgesia improved up to 3 hr after recovery. This is consistent with the analgesic effect of tramadol lasted for 4 hr after intravenous administration in 11 parrots when given at the dose of 5 mg kg^{-1}.[14]

Table 2. The duration and amplitudes of waves (PQRST) in lead II and heart rate in anesthetized buzzards in the experimental treatments.

Parameters	KT	KM	KD	KX	KMT	KDT	KXT
P (sec)	0.02 ± 0.00	0.02 ± 0.00	0.02 ± 0.00	0.03 ± 0.00	0.01 ± 0.00	0.02 ± 0.00	0.03 ± 0.00
P (mV)	0.11 ± 0.03	0.09 ± 0.03	0.12 ± 0.02	0.11 ± 0.02	0.10 ± 0.03	0.11 ± 0.03	0.18 ± 0.03
QRS (sec)	0.04 ± 0.00	0.04± 0.00	0.04 ± 0.00	0.04 ± 0.00	0.04 ± 0.01	0.04 ± 0.00	0.04 ± 0.00
QRS (mV)	0.42 ± 0.07	0.48 ± 0.14	0.35 ± 0.06	0.32 ± 0.08	0.43 ± 0.08	0.33 ± 0.07	0.36 ± 0.09
P-R Interval (sec)	0.34 ± 0.10	0.38 ± 0.10	0.44 ± 0.07	0.50 ± 0.04	0.38 ± 0.10	0.48 ± 0.08	0.52 ± 0.05
T (mV)	0.38 ± 0.06	0.42 ± 0.04	0.33 ± 0.03	0.33 ± 0.07	0.37 ± 0.09	0.31 ± 0.03	0.29 ± 0.04
T (sec)	0.06 ± 0.00	0.06 ± 0.00	0.06 ± 0.00	0.06 ± 0.00	0.05 ± 0.00	0.05 ± 0.00	0.05 ± 0.00
Heart rate	346.10 ± 27.60*	389.60 ± 59.20*	379.40 ± 21.27*	154.00 ± 21.21	375.20 ± 64.91*	387.20 ± 35.41*	207.20 ± 35.48

* Asterisk indicates a significant difference compared to KX group ($p < 0.05$).
KT: Ketamin-Tramadol, KM: Ketamine-Midazolam, KD: Ketamine-Diazepam, KX: Ketamine-Xylazine, KMT: KM-Tramadol, KDT: KD-Tramadol, and KXT: KX-Tramadol.

Table 3. The evaluation of analgesia quality in experimental groups including Ketamine (K), Xylazine (X), Diazepam (D), Midazolam (M), Tramadol (T) by thermal design in 45 °C before anesthesia (A), during anesthesia (B), 30 min after recovery (C), 90 min after recovery (D) and 180 min after recovery (E), (Number of buzzards).

Protocols	Excellent (response ≥ 10 sec)					Good (response > 5sec or <10 sec)					Poor (response ≤ 5sec)				
	A	B	C	D	E	A	B	C	D	E	A	B	C	D	E
KX	-	5	2	-	-	-	5	3	2	1	10	-	5	8	9
KXT	-	5	4	4	4		5	5	5	5	10	-	1	1	1
KD	-	3	1	-	-	-	5	2	2	-	10	1	7	8	10
KDT	-	5	5	3	3	-	5	5	6	6	10	-	-	1	1
KM	-	4	2	-	-	-	6	4	3	1	10	-	4	7	10
KMT	-	5	5	4	3	-	5	5	5	5	10	-	-	1	2
KT	-	5	5	5	2	-	5	5	5	6	10	-	-	-	2

KT: Ketamin-Tramadol, KM: Ketamine-Midazolam, KD: Ketamine-Diazepam, KX: Ketamine-Xylazine, KMT: KM-Tramadol, KDT: KD-Tramadol, and KXT: KX-Tramadol.

There are few reports using tramadol to produce balanced anesthesia in birds.[17,18] However, in layer chickens, it has been found that tramadol at two doses of 5.00 and 10.00 mg kg^{-1} with ketamine caused anesthesia with a little effect on the heart rate.[19]

In order to achieve reliable anesthesia, a suitable treatment protocol should induce smooth anesthesia and fast recovery. Long recoveries are associated with hypothermia and hypoxia.[28] There are many studies in the literature about clinical evaluation of injection anesthesia in different routes in birds.[4-7,19,24,28-31] In our study, the onset of anesthesia was rapid in all experimental treatment, whereas the recovery time was not rapid in the KT, KX and KXT treatment protocols compared to the other protocols. In addition to these factors, the quality of recovery can be vital in birds. The quality of recovery is graded based on struggle, walking with assistance and ataxia degree at the end of anesthesia maintenance. The quality of recovery in the experimental anesthesia treatment protocols was unsuitable in ketamine-xylazine and ketamine-tramadol combinations. Thus, the physical restraint was required as struggle and wing flapping could injure birds in these treatment protocols.

Electrocardiography is a non-invasive technique widely used in the study of cardiac pathophysiology. Sedation and anesthesia may influence several ECG values for waves and intervals as well as cardiac rhythm and heart rate.[32] Morphological patterns and values of PQRS-T deflections in all leads obtained from applied anesthesia treatment protocols were largely in agreement with the ECG of conscious golden eagles and buzzards anesthetized with isoflurane.[3,32] The mean heart rate ranged from 154.00 ± 21.21 to 389.60 ± 59.20 beats min^{-1} in this study. The mean heart rates of conscious golden eagles and anesthetized buzzards (*Buteo buteo*) were 346.76 ± 14.29 beats min^{-1} and 325.26 ± 52.90 beats min^{-1}, respectively.[3,32] Eyarefe and Oguntoye have used tramadol at two doses of 5 and 10 mg kg^{-1} in layer chickens and observed that it had little effect on the heart rate.[19] Thus, it could be concluded that the use of xylazine can cause bradycardia in buzzard. Moreover, a decrease in the heart rate and an increase in the P-R interval of the birds in KX and KXT treatment protocols were observed. The results also revealed a negative relationship between heart rate and P-R interval, which was in agreement with the results of the Espino *et al*.[3] Xylazine is a non-narcotic, sedative, muscle relaxant and analgesic alpha-2-adrenergic agonist that has been used in a wide range of wild and domestic animals and birds.[7,29] It sometimes fails to immobilize birds or causes significant cardiopulmonary side effects.[30,31] An advantage of the use of alpha-2-agonists alone or in combination with other drugs is its reversibility with the alpha-2-antagonists, atipamezole and yohimbine.[2]

Regarding the other parameters of ECG, there was no significant difference between the experimental treatment protocols. Only a cardiac arrhythmia was observed in a single buzzard anesthetized through KX treatment protocol. By adding tramadol to the anesthesia protocols, the ECG values of waves, P-T interval and heart rate were either slightly elevated or reduced. However, an organized decrease was observed in the amplitude and duration of T wave in the KM, KD and KX treatment protocols after the administration of tramadol. Intra-muscular administration of tramadol at 1 mg kg^{-1} bodyweight in the Kagani goats caused a reduction in T-wave amplitude at first 30 min.[33] The increase of T wave amplitude and duration was observed in the shocked and electrocution raptors and ducks that had the sign of hyperkalemia.[34,35] These parameters were higher than those in the buzzards anesthetized with isoflurane.[3] This difference may be attributed to the geographical zone or anesthesia drug.

Tramadol is a synthetic analogue of codeine,[36] but less expensive. It is a centrally acting opiate analgesic that has not been well studied in different avian species.[27] In our study, tramadol was administered intra-muscularly. Tramadol at doses of 5.00 and 30.00 mg kg^{-1} has induced suitable analgesia in bald eagles and parrots by oral administration. Tramadol (4.00 mg kg^{-1} intra-venous) has induced analgesia in eagles, but the analgesic effect was short in comparison with oral route. In young pigs, tramadol has improved the quality of anesthesia induction and increased the duration of antinociception in KX treatment protocol without increasing the duration of

anesthesia, nor causing additional depression of the measured physiological parameters.[37] Although, a transient bradycardia for 10 min immediately following intra-venous administration of tramadol in bald eagles has been reported and significant adverse side effects have not been reported in other avian species used in tramadol related investigations. During the study, the adverse effect of tramadol was not observed. Clinical examination and monitoring of the buzzards for two weeks after anesthesia revealed no adverse effect and they were finally returned to nature.

Anesthesia with ketamine-tramadol and ketamine-xylazine at the commonly used doses is not recommended for balanced anesthesia in buzzards. The quality of recovery and duration of anesthesia were not suitable in KT treatment protocol. Moreover, the cardiopulmonary depression caused by ketamine-xylazine and poor quality of recovery can increase the fatality risk of buzzard anesthesia. Therefore, xylazine must be used for birds when its antagonists such asatipamezole and yohimbine are easily accessible. Tramadol does not have substantial effects on anesthesia times and ECG parameters. It has an analgesic effect up to 4 hr in buzzards when used with ketamine-benzodiazepines or KX combinations. So, tramadol can be used with injectable anesthetics to make suitably balanced anesthesia.

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Conflict of interest

The authors declare that there is no conflict of interest.

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